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EXAMINER	
SALMON, KATHERINE D	

ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
08/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/786,518	GREINWALD ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-23 and 25-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-23, 25-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

1. This action is in response to papers filed 6/01/2009.

2. Claims 17-23, 25-37 are pending. Claims 1-16 and 24 have been cancelled.

3. The following rejections are reiterated. Response to arguments follows.

4. This action is FINAL.

Withdrawn Rejections

5. The rejection of claim 29 under 35 USC 112/2nd paragraph made in section 5 of the previous office action (12/01/2008) is moot based upon amendments to the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 17-23, 25-27, 29-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5474796 December 12, 1995).

With regard to Claim 17, Brennan teaches an array (column 9 lines 49-50). Brennan teaches that the array comprises nucleic acids which contains oligonucleotides with 10 nucleotides each (Column 9, lines 49-50). Brennan teaches the total array represents every possible permutation of the 10-mer oligonucleotide (Column 9, lines 53-55). Therefore the array comprises nucleic acids in which the sequences are found

in CDH23, MYO7A, OTOF, SLC26A4, and USH2A. The phrase “indicative of presence or absence of an allele associated with a risk for hearing loss” is an intended use of the structure but provides no structural limitations.

With regard to Claims 18-21 and 34-37, Brennan teaches an array representing every possible permutation of the 10-mer oligonucleotide (Column 9, lines 53-55) and therefore comprises sequences found in multiple adjacent exons and single exons.

With regard to Claim 22, the term “kit” provides no structural limitations to distinguish the term from a teaching of a microarray and buffers and components. The preamble “detecting a candidate gene responsible for hearing loss” is not given any patentable weight and is an intended use of the claimed kit. Any microarray composed of the structural limitations of the claim could be used to detect a candidate gene responsible for hearing loss. Brennan et al. teaches a microarray (column 9 line 58) and buffers and components (Column 9 lines 60-65).

With regard to Claim 23, Brennan teaches a microarray comprising a solid support comprising a plurality of capture nucleic sequences (column 9 lines 53-55). The phrase "wherein the contacting permits hybridization under stringent conditions...for hearing loss" is an intended use of the claimed kit and provides no structural limitation.

With regard to Claim 25, Brennan teaches nucleic acids which would include a set of 10-mer fragments of the genetic sequences found in CDH23, MYO7A, OTOF, SLC26A4, and USH2A (column 9 lines 60-65).

With regard to Claim 26, Brennan teaches a microarray comprising a set of probes that of every possible permutation of the 10-mer oligonucleotide (Column 9,

lines 53-55). Therefore the microarray would include a set of probes for allelic variants of CDH23, MYO7A, OTOF, SLC26A4, and USH2A.

With regard to Claim 27, Brennan teaches a microarray comprised of oligonucleotide probes (column 9 line 18).

With regard to Claim 29, Brennan teaches the nucleic acid molecules are bound to a solid support (column 9 line 57).

With regard to Claim 30 and 33, Brennan teaches a microarray comprising a set of probes that of every possible permutation of the 10-mer oligonucleotide (Column 9, lines 53-55). Therefore the microarray would include a set of probes for allelic variants of CDH23, MYO7A, OTOF, SLC26A4, and USH2A.

With regard to Claims 31-32, because Brennan teaches every possible permutation of the 10-mer oligonucleotides the microarray would comprise perfect match, mismatches and deletion mutants.

Response to arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is set forth below with response to arguments following.

(A) The reply asserts that Brennan does not teach "an array representing every possible permutation of the 10 mer oligonucleotide" but rather it teaches the construction of 10 mer oligonucleotides complementary to a known nucleic acid (p. 6 1st paragraph). The reply asserts that as shown in Example 4 and Figure 1c the construction of a particular permutation of 10 mer is based on moving in a 5' to 3'

direction and determining every possible 10 mer in the context of a particular target nucleic acid (p. 6 2nd full paragraph).

These arguments have been fully reviewed but have not been found persuasive.

The reply seems to be asserting that Brennan only teaches the permutation of a particular target, however, Brennan teaches an array comprised of every possible permutation of the 10 mer. Regardless of the starting target sequence, because Brennan teaches determining every possible permutation, the array would be comprised of every 10 mer which could be made. Therefore these 10 mers would encompass 10 mer fragments of the claimed genes. The reply teaches that one in the art could vary the positions at each position of a 10-mer oligonucleotide to generate all 1,048,576 but the Figure in 1c only shows construction of 3mer oligonucleotides complementary to a known target (p. 6 2nd fully paragraph). However, figures in the patent of Brennan do not limit the teaching of Brennan. Brennan teaches that all possible 10 mers can be placed on an array, and as such encompasses the microarray claimed in the instant application.

(B) The reply asserts that Brennan does not teach "a diagnostic microarray", "a set of hearing loss sequences", that these hearing loss sequences "are indicative of presence or absence of an allele associated with a risk for hearing loss" and does not teach that the set "consists essentially of genetic sequences found in CDH23, MYO7A, OTOF, SLC26A4, and USH2A genes" (p. 6 last paragraph).

These arguments have been fully reviewed but have not been found persuasive.

Although Brennan does not specifically teach these phrases, these phrases do not limit the scope of the claims such that Brennan would not broadly encompass the microarray claimed. The term "diagnostic microarray" is not clearly defined in the instant specification, and therefore it is interpreted as any microarray which could be used to diagnose. Brennan teaches an array which is comprised of all possible 10 mers, therefore, it could be used to detect various target sequences related to diagnosis of diseases. As such Brennan et al. teaches the functional components of the claimed microarray which would be diagnositive. With regard to "a set of hearing loss sequences" and “consists essentially of genetic sequences found in CDH23, MYO7A, OTOF, SLC26A4, and USH2A genes”, Brennan teaches every possible 10 mer sequence and therefore would encompass sequences which were specific to CDH23, MYO7A, OTOF, SLC26A4, and USH2A genes. As the term "consisting essentially of" is not clearly defined in the instant specification, the claim is being interpreted as comprising language and as such the array of Brennan would comprises sequences found in CDH23, MYO7A, OTOF, SLC26A4, and USH2A genes. The phrase “indicative of presence or absence of an allele associated with a risk for hearing loss” is an intended use of the structure but provides no structural limitations. Any sequence fragment could be used to determining the presence or absence of an allele.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 17, 22-23, 25-27, 29-30, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morton et al. (Human Molecular Genetics 2002 Vol. 11 p. 1229) in view of Choo et al. (The Journal of Pediatrics February 2002 p. 148).

With regard to Claim 17, Morton et al. teaches that hundreds of syndromic forms of deafness have been described and the underlying genetic mutation identified for many of the common forms (p. 1231 1st sentence). In Table 1, Morton et al. lists 58 genes associated with hearing loss (claims 7-12). Morton et al. teaches a range of

genes for both syndromic and nonsyndromic hearing loss (Table 1). Morton et al. teaches genes of CDH23, MYO7A, OTOF, SLC26A4, and USH2A (Table 1). Morton et al. teaches that these genes comprise genetic mutations for many forms of hearing loss (p. 1231 1st sentence and p. 1232 1st column 2nd paragraph). Therefore Morton et al. teaches nucleic acid sequences which comprise a set of hearing loss sequences (e.g. Table 1) wherein the set consists essentially of nucleic acid sequences found in CDH23, MYO7A, OTOF, SLC26A4, and USH2A. The term “consists essentially" has not been defined by the specification and therefore is broadly interpreted as comprising.

With regard to Claim 25 the limitation that the set “consists" of genetic sequences found in CDH23, MYO7A, OTOF, SLC26A4, and USH2A does not limit the nucleic acids on the microarray because the microarray “comprise nucleic sequences wherein said sequences comprise of a set of hearing loss genes”. Therefore the microarray can include nucleic acids sequences from other genes besides the set of CDH23, MYO7A, OTOF, SLC26A4, and USH2A. Therefore Morton et al. teaches nucleic acid sequences (Table 1) which comprise a set of sequences consisting of CDH23, MYO7A, OTOF, SLC26A4, and USH2A.

With regard to Claim 26, Morton et al. teaches the set of nucleic acids includes probes for variants of hearing loss genes (p. 1232 1st column 2nd paragraph). Morton et al. lists 58 genes associated with hearing loss (claims 7-12). Morton et al. teaches a range of genes for both syndromic and nonsyndromic hearing loss (Table 1). Morton et al. teaches genetic mutations from CDH23, MYO7A, OTOF, SLC26A4, and USH2A (Table 1). Therefore Morton et al. teaches nucleic acid sequences which comprise a

set of hearing loss sequences (e.g. Table 1) wherein the set consists essentially of nucleic acid sequences found in CDH23, MYO7A, OTOF, SLC26A4, and USH2A. The term “consists essentially" has not been defined by the specification and therefore is broadly interpreted as comprising.

With regard to Claim 30, Morton et al. teaches that the genes comprise mutations (e.g. allelic variants) which are associated with hearing loss (p. 1231 last paragraph and p. 1232 1st paragraph). Choo et al. as discussed below teaches that such allelic variants can be made into cDNA probes and spotted onto an array (p. 149 3rd column 1st paragraph).

With regard to Claim 33, the limitation that the set “consists" of genetic sequences found in CDH23, MYO7A, OTOF, SLC26A4, and USH2A does not limit the nucleic acids on the microarray because the microarray comprises nucleic sequences wherein said sequences comprise a set of hearing loss genes. Therefore the microarray can include nucleic acids sequences from other genes besides the set of CDH23, MYO7A, OTOF, SLC26A4, and USH2A. Therefore Morton et al. teaches nucleic acid sequences (Table 1) which comprise a set of sequences consisting of CDH23, MYO7A, OTOF, SLC26A4, and USH2A.

Morton et al., however, does not teach a microarray comprising these genetic mutations.

Choo et al. teaches that molecular genetics will affect clinical management of pediatric sensorineural hearing loss. With regard to Claim 17, Choo et al. teaches that a “deafness gene chip” could be developed to screen newborns for gene mutations that

cause or predispose that infant to significant hearing impairment (p. 149 2nd column last sentence and 3rd column 1st paragraph). Choo et al. teaches DNA would be screened on a microarray spotted with cDNAs or oligonucleotides associated with hearing loss (p. 149 3rd column 1st paragraph). Therefore Choo et al. teaches a microarray and guidance to place hearing loss sequences onto the microarray.

With regard to Claim 22, the term “kit” provides no structural limitations to distinguish the term from a teaching of a microarray and buffers and components. The preamble “detecting a candidate gene responsible for hearing loss” is not given any patentable weight and is an intended use of the claimed kit. Choo et al. teaches a microarray and buffers and components (p. 149 2nd column last sentence and 3rd column 1st paragraph).

With regard to Claim 23, Choo et al. teaches a microarray comprising a solid support comprising a plurality of capture nucleotide sequences (p. 149 2nd column last sentence and 3rd column 1st paragraph). Choo et al. teaches that a sample from a patient is contacted (p. 149 3rd column 1st paragraph). The phrase "wherein the contacting permits hybridization under stringent conditions...for hearing loss" is an intended use of the claimed kit and provides no structural limitation.

With regard to Claim 27, Cho et al. teaches placing cDNA molecules (e.g. oligonucleotide probes) onto an array (p. 149 2nd column last sentence and 3rd column 1st paragraph).

With regard to Claim 29, Choo et al. teaches placing nucleic acid molecules on an microarray (e.g. a solid support) (p. 149 2nd column last sentence and 3rd column 1st

paragraph).

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the list of genes of Morton et al. to attach the sequences to a microarray to form a "deaf chip" as taught by Choo et al. to screen for hearing loss with a reasonable expectation of success. The ordinarily artisan would be motivated to place sequences of known mutations associated with deafness as taught by Morton et al. onto a microarray as taught by Choo et al. because Choo et al. teaches that microarray technology allows investigators to simultaneously assay the expression of hundreds or thousands of genes (p. 149 2nd column last paragraph). Choo et al. teaches that it is very apparent that a “deafness gene chip” could be developed for purposes of screening newborns for gene mutations that cause or predispose that infant to significant hearing impairment (p. 149 2nd column last paragraph and 3rd column 1st paragraph). Choo et al. further teaches that “deafness gene chips” allows for more cost-effective, efficient newborn hearing screening with the use of molecular techniques (p. 149 3rd column). Therefore the ordinary artisan would be motivated to place the sequences of known gene mutations comprising sequences found in CDH23, MYO7A, OTOF, SLC26A4, and USH2A as taught by Morton et al. onto an array as taught by Choo et al. to screen patients with a large number of gene mutations quickly and efficiently.

Response to arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is set forth below with response to arguments following.

(A) The reply asserts that that the transitional phrase "consisting essentially of" has a well established meaning of occupying a middle ground between claims that recite the transitional phrase “consisting of” and comprising (p. 7 last paragraph). The reply asserts that the term “consisting essentially of" limits the scope of the claim to specific materials or steps which materially affect the basic and novel characteristics of the invention (p. 7 last paragraph-p. 8 1st paragraph). The reply asserts that the basic and novel characteristics of the claimed microarrays is the selection of hearing loss sequences specifically found in CDH23, MYO7A, OTOF, SLC26A4 and USH2A (p. 8 2nd paragraph). The reply asserts that Morton et al. provides a generic list of 58 genes which include many that are not recited by the instant claims (p. 8 2nd paragraph).

These arguments have been fully reviewed but have not been found persuasive.

The instant specification does not define the term “consisting essentially of”. Although consisting essentially of limits the scope to specific materials or steps which materially affect the basic and novel characteristics of the invention, because of lack of guidance in the specification these specific materials can be broadly interpreted. Although the selection of hearing loss sequences specifically found in CDH23, MYO7A, OTOF, SLC26A4 and USH2A could be considered a specific material, there are many other interpretations of the term. An array or a collection of hearing loss genes such as those taught by Morton et al could also be considered specific materials. As such the instant specification has not provided any explicit guidance as what would be considered “specific materials or steps which materially

affect the basic and novel characteristics of the invention". The MPEP in section 2111.03[R-3] makes clear

> " For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also AK Steel Corp. v. Sollac, 344 F.3d 1234, 1240-41, 68 USPQ2d 1280, 1283-84 (Fed. Cir. 2003)".

The MPEP further states that the applicant has the burden of showing that the introduction of additional components would materially change the characteristics of applicant's invention. Herein in the instant case additional mutations related to deafness genes would not change the invention, as the microarray would still be comprised of diagnostive components which detect hearing loss. The instant reply has not set forth any argument that the addition of other hearing loss genes would materially change the characteristics of applicant's invention.

9. Claims 18-21, 32 and 34-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morton et al. (Human Molecular Genetics 2002 Vol. 11 p. 1229) in view of Choo et al. (The Journal of Pediatrics February 2002 p. 148) as applied to claims 17, 22-23, 25-27, 29-30, and 33 and in view of Weston et al. (American Journal Human Genetics 1996 Vol 59 p. 1074).

The combination of Morton et al. and Choo et al. teach a microarray comprising sequences from the group consisting of genetic sequences from CDH23, MYO7A,

OTOF, SLC26A4, and USH2A. The combination of Morton et al. and Choo et al. does not teach that the sequences comprise multiple adjacent exon or single exon.

Weston et al. teaches screening of patients with mutations in MYO7A (abstract). With regard to Claims 18-19 and 34-35, Weston et al. teaches detection of mutations of MYO7A within adjacent exon (Exon 13 and 14) (Table 2). Therefore Weston et al. teaches that the set comprises sequences found in multiple adjacent exons because Weston et al. teaches multiple exons (13 and 14) which are adjacent.

With regard to Claims 20-21 and 36-37, Weston et al. teaches mutations which are present in only one exon (e.g. EXON 3 or 4) (Table 2). Therefore Weston et al. teaches various mutations of MYO7A which are in single exon and are found in a combination of adjacent exon.

With regard to Claim 32, Weston et al. teaches that allelic variants in MYO7A include a deletion mutation (p. 1077 Table 2).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention was made to detect any of the mutations of MYO7A in single exon and adjacent exon taught by Weston et al. by a microarray comprising sequences as taught by Morton et al. and Choo et al. with a reasonable expectation of success. The ordinary artisan would be motivated to design sequences on the microarray of Morton et al. and Choo et al. comprising single exon and adjacent exon taught by Weston et al. because Weston et al. teaches that these mutations are associated with hearing loss (abstract). Therefore the ordinary artisan would be

motivated to detect on associated the single exon and adjacent exon of MYO7A as taught by Weston et al. to screen patients for genetically associated hearing disorders.

Response to Arguments

The reply traverses the rejection. A summary of the arguments set forth in the reply is provided below with response to arguments following.

The reply asserts that Weston does not supplement the deficiencies of Morton et al. and Choo et al. (p. 8 last paragraph and p. 9 1st paragraph).

This argument has been fully reviewed but has not been found persuasive.

As discussed in the 35 USC 103(a) rejections of Morton et al. in view of Choo et al. the combination of art teaches all the structural limitations of the pending claims.

10. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morton et al. (Human Molecular Genetics 2002 Vol. 11 p. 1229) in view of Choo et al. (The Journal of Pediatrics February 2002 p. 148) as applied to Claims 17, 22-23, 25-27, 29-30, and 33 and further in view of Hogan (US Patent 5541308 July 30, 1996).

Morton et al. and Choo et al. teaches a microarray comprising a plurality of nucleic molecules wherein said nucleic acid molecules a set of probes for allelic variants of hearing loss, but does not teaches that the oligonucleotide probes are 20-25 nucleotides in length.

Hogan et al. provides guidance for making probes. Hogan teaches guidance for

the selection of primers and probes. Hogan et al. teaches the use of specific primers and probes to amplify the 16S region of bacteria. Hogan et al. provides guidance for the selection of probes.

> "Once the variable regions are identified, the sequences are aligned to reveal areas of maximum homology or 'match'. At this point, the sequences are examined to identify potential probe regions. Two important objectives in designing a probe are to maximize homology to the target sequence(s) (greater than 90% homology is recommended) and to minimize homology to non-target sequence(s) (less than 90% homology to non-targets is recommended). We have identified the following useful guidelines for designing probes with the desired characteristics.
> Fist, probes should be positioned so as to minimize the stability of the probe: nontarget nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarily to non-target organisms, avoiding G and C rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible (for example, dG:rU base pairs are less destabilizing than some others). Second, the stability of the probe: target nucleic acid hybrid should be maximized. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G: C base pairs and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %G and %C result in a Tm about 2-10 ºC higher than the temperature at which the final assay will be performed. The importance and effect of various assay conditions will be explained further herein. Third, regions of the rRNA which are known to form strong structure inhibitory to hybridization are less preferred. Finally probes with extensive self complementarity should be avoided." (See Column 6 lines 66-67 and Column 7 lines 1-29).

Hogan et al. teaches, "while oligonucleotide probes of different lengths and base composition may be used, oligonucleotide probes preferred in this invention are between about 15 and about 50 bases in length" (see Column 10, lines 13-15). Therefore Hogan et al. teaches taking a sequence and fragmenting the sequence into smaller oligonucleotides to be used as probes. Hogan et al. teaches that these probes are preferable to be between about 15 and about 50 bases in length.

Therefore, the ordinary artisan would have been motivated to select any number of oligonucleotide fragments including probes that were 20-25 nucleotides in length from the allelic variant areas of CDH23, MYO7A, OTOF, SLC26A4, and USH2A. The art of designing probes at the time the invention was made was very well described in the art. Designing probes is routine experimentation. The prior art teaches the parameters and objectives involved in the selection of oligonucleotides that function as probes, see Hogan et al. The claimed probes are prima facie obvious over the cited references in the absence of secondary considerations, given the extensive teachings in the art. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to immobilize probes of 20 to 25 nucleotides in length to the microarray taught by Morton et al. and Choo et a

Response to Arguments

The reply traverses the rejection. A summary of the arguments set forth in the reply is provided below with response to arguments following.

The reply asserts that Hogan does not supplement the deficiencies of Morton et al. and Choo et al. (p. 8 last paragraph and p. 9 1st paragraph).

This argument has been fully reviewed but has not been found persuasive.

As discussed in the 35 USC 103(a) rejections of Morton et al. in view of Choo et al. the combination of art teaches all the structural limitations of the pending claims.

11. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morton et al. (Human Molecular Genetics 2002 Vol. 11 p. 1229) in view of Choo et al. (The Journal of Pediatrics February 2002 p. 148) as applied to Claims 17, 22-23, 25-27, 29-30, and 33 and further in view of Chee et al. (WO1995/011995).

Morton et al. and Choo et al. teaches a microarray comprising a plurality of nucleic molecules wherein said nucleic acid molecules a set of probes for allelic variants of hearing loss, but does not teaches that the microarray comprises perfect match and mismatches.

Chee et al. teaches guidance to design arrays to detect differences in targets (p. 2 line 21). Chee et al. teaches probes made which include the nucleotide of interest (e.g. variant) (p. 25 lines 1-11). Chee et al. teaches that the probe sets comprise probes exhibiting prefect complementary with a selected reference sequence (p. 21 lines 30-31).

Therefore it would be prima facie obvious to one of skill in the art at the time of filing to modify the microarray of Morton et al. and Choo et al. to include probes with perfect matches to the nucleotide of interest and mismatches of the allelic variants as taught by Chee. The ordinary artisan would be motivated to immobilize both a perfect match probe and a mismatch probe in order to determine if the sample has an allelic variant at a particular gene or if the sample does not comprise the allelic variant (e.g. hybridize to the perfect match).

Response to Arguments

The reply traverses the rejection. A summary of the arguments set forth in the reply is provided below with response to arguments following.

The reply asserts that Chee does not supplement the deficiencies of Morton et al. and Choo et al. (p. 8 last paragraph and p. 9 1st paragraph).

This argument has been fully reviewed but has not been found persuasive.

As discussed in the 35 USC 103(a) rejections of Morton et al. in view of Choo et al. the combination of art teaches all the structural limitations of the pending claims.

Conclusion

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE SALMON whose telephone number is

(571)272-3316. The examiner can normally be reached on Monday-Friday 8AM-530PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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